AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the applications:

Listing of Claims:

Claims 1-52 canceled.

53. (currently amended) A method for assaying hu-Asp1 α-secretase activity comprising the steps of:

(a) contacting hu-Asp1 enzyme with an amyloid precursor protein (APP) substrate, wherein the hu-Asp1 enzyme is a recombinant polypeptide expressed by a host cell transformed or transfected with a nucleic acid molecule that comprises a nucleotide sequence that encodes an amino acid sequence at least 95% identical to SEQ ID NO: 2 or to a fragment of SEQ ID NO: 2 that retains α-secretase activity, wherein the polypeptide retains α-secretase activity, and wherein said substrate contains an α-secretase cleavage site; and

(b) measuring cleavage of the APP substrate at the α-cleavage site, thereby assaying hu-Asp1 α-secretase activity.

54. (canceled)

55. (currently amended) A method ~~of claim 54~~ for assaying hu-Asp1 α-secretase activity comprising the steps of:

(a) contacting a hu-Asp1 enzyme with an amyloid precursor protein (APP) substrate, wherein said substrate contains an α-secretase cleavage site, wherein the hu-Asp1 enzyme is a purified and isolated ~~from said cell~~ polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 2 or to a fragment of SEQ ID NO: 2 that retains α-secretase activity, wherein the polypeptide retains α-secretase activity; and

(b) measuring cleavage of the APP substrate at the α-cleavage site, thereby assaying hu-Asp1 α-secretase activity.

56. (currently amended) A method according to any one of claims 53, 55, 79 or 80 ~~claim 54~~, wherein the ~~polynucleotide sequence encodes a~~ polypeptide ~~that comprises the hu-Asp1 amino acid sequence set forth in SEQ ID NO: 2 or a fragment thereof, wherein said fragments retains α-secretase activity~~ lacks a transmembrane domain.

57. (currently amended) A method according to claim [[54]] 78, wherein the ~~polynucleotide sequence encodes a hu-Asp1 amino acid sequence lacking~~ the polypeptide lacks transmembrane amino acids 469-492 of SEQ ID NO: 2.

58. (currently amended) A method according to claim 57, wherein the ~~polynucleotide sequence encodes a hu-Asp1 amino acid sequence~~ polypeptide further ~~lacking~~ lacks the cytoplasmic domain amino acids 493-518 of SEQ ID NO: 2.

59. (currently amended) A method according to ~~any one of claims 55~~ claim 57, wherein the ~~hu-Asp1~~ polypeptide further lacks amino terminal amino acids 1-62 of SEQ ID NO: 2.

60. (currently amended) A method according to claim 53 or 79 wherein the contacting step comprises growing ~~a~~ the host cell ~~transfected or transformed with a polynucleotide encoding hu-Asp1 enzyme or a fragment thereof that retains hu-Asp1 α-secretase activity, wherein the cell is grown~~ under conditions in which the cell expresses the hu-Asp1 enzyme in the presence of the APP substrate.

61. (currently amended) A method of claim 60, wherein said cell further expresses a polynucleotide encoding an APP substrate containing an α-secretase cleavage site, and wherein the contacting step further comprises growing the cell under conditions in which the cell expresses the hu-Asp1 enzyme and the APP substrate.

62. (currently amended) A method ~~of claim~~ according to any one of claims 53, 55, 79 and 80 wherein the APP substrate α-secretase cleavage site comprises the amino acid sequence LVFFAEDF (SEQ ID NO: 84) or KLVFFAED (SEQ ID NO: 73).

63. (currently amended) A method of ~~claims~~ claim 62, wherein the APP substrate comprises a detectable label.

64. (currently amended) A method of claim [[53]] 63, wherein the detectable label is selected from the group consisting of radioactive labels, enzymatic labels and ~~flourescent~~ fluorescent labels.

65. (currently amended) A method ~~of claim~~ according to any one of claims 53, 55, 79 and 80 wherein the APP substrate comprises a human APP isoform and further comprises a carboxy-terminal di-lysine.

66. (currently amended) A method ~~of claim~~ according to any one of claims 53, 55, 79 and 80, wherein the APP substrate comprises a human APP isoform and the determining step comprises measuring the production of amyloid alpha peptide (sAPPα).

67. (currently amended) A method ~~of claim~~ according to any one of claims 53, 55, 79 and 80, wherein the method further comprises steps of:

(c) determining the level of hu-Asp1 α-secretase activity in the presence and absence of a modulator of hu-Asp1 α-secretase activity; and

(d) comparing the hu-Asp1 α-secretase activity in the presence and absence of the modulator, wherein modulators that increase hu-Asp1 α-secretase activity are identified as candidate Alzheimer's disease therapeutics.

Claims 68-77 (canceled)

78. (currently amended) A method ~~of claim 54~~ according to any one of claims 53, 55, 79 and 80, wherein the ~~polynucleotide sequence encodes a hu-Asp1 amino acid sequence comprising~~ the polypeptide comprises amino acids 63-468 of SEQ ID NO: 2.

79. (new) A method for assaying hu-Asp1 α-secretase activity comprising the steps of:

(a) contacting a hu-Asp1 enzyme with an amyloid precursor protein (APP) substrate, wherein said substrate contains an α-secretase cleavage site, wherein the hu-Asp1 enzyme is a recombinant polypeptide having α-secretase activity, and wherein said polypeptide is expressed by a host cell transformed or tranfected with a nucleotide sequence that encodes the polypeptide and hybridizes under the following stringent conditions to the complement of SEQ ID NO: 1:

(1) hybridization at 42°C in a hybridization buffer comprising 6x SSC and 0.1% SDS, and

(2) washing at 65°C in a wash solution comprising 1x SSC and 0.1% SDS; and

(b) measuring cleavage of the APP substrate at the α-cleavage site, thereby assaying hu-Asp1 α-secretase activity.

80. (new) A method for assaying hu-Asp1 α-secretase activity comprising the steps of:

(a) contacting a hu-Asp1 enzyme with an amyloid precursor protein (APP) substrate, wherein the substrate contains an α-secretase cleavage site, wherein the hu-Asp1 enzyme is a purified and isolated polypeptide comprising an amino acid sequence encoded by a nucleotide sequence that hybridizes under the following stringent conditions to the complement of SEQ ID NO: 1:

(1) hybridization at 42°C in a hybridization buffer comprising 6x SSC and 0.1% SDS, and

(2) washing at 65°C in a wash solution comprising 1x SSC and 0.1% SDS; and

(b) measuring cleavage of the APP substrate at the α-cleavage site, thereby assaying hu-Asp1 α-secretase activity.

81. (new) A method for assaying hu-Asp1 α-secretase activity comprising the steps of:

(a) contacting a hu-Asp1 enzyme with a amyloid precursor protein (APP) substrate, wherein the hu-Asp1 enzyme is a polypeptide with α-secretase activity, wherein the polypeptide comprises an amino acid sequence at least 95% identical to SEQ ID NO: 2 or to a fragment of SEQ ID NO: 2 that retains α-secretase activity, wherein said substrate is a human APP isoform comprising an α-secretase cleavage site and a carboxy di-lysine; and

(b) measuring cleavage of the APP substrate at the α-cleavage site, thereby assaying hu-Asp1 α-secretase activity.